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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,596	05/17/2006	Shun-ichi Harada	21351YP	9402
210	7590	01/18/2008	EXAMINER	
MERCK AND CO., INC			GAMETT, DANIEL C	
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RAHWAY, NJ 07065-0907			PAPER NUMBER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/579,596	Applicant(s) HARADA ET AL.	
	Examiner DANIEL C. GAMETT	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 10-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 10-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 May 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>04/19/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The preliminary amendments of 05/17/2006 have been entered in full. Claims 7-9 and 16-37 are cancelled. Claims 1-6 and 10-15 are under examination.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1-6 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Application Publication 20030068312 (McCarthy), filed October 4, 2001 (of record). Claims 1-6 are drawn to an isolated nucleic acid molecule comprising a nucleotide sequence encoding a cynomolgus monkey Dickkopf-4 (cDkk-4) protein which has an amino acid sequence as set forth in SEQ ID NO:2 (claims 1-4), wherein the nucleic acid has a nucleotide sequence as set forth in SEQ ID NO:1 (claim 5) and to an isolated protein comprising an amino acid sequence as set forth in SEQ ID NO:2 (claim 6). The limitations “a nucleotide sequence” (claims 1 and 5) or “an amino acid sequence” (claims 1 and 6) can be met by the occurrence of a little as two consecutive nucleotides or amino acids that are identical to the

reference sequence. The 20030068312 application discloses SEQ ID NO: 4, a nucleic acid

which is 94.5 % identical to SEQ ID NO:1, as shown by the following alignment:

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US-09-972-473-4
; Sequence 4, Application US/09972473
; Publication No. US20030068312A1
; GENERAL INFORMATION:
;  APPLICANT: McCarthy, Sean A.
;  TITLE OF INVENTION: NOVEL HUMAN DICKKOPF-RELATED PROTEIN AND NUCLEIC ACID
;  TITLE OF INVENTION:  MOLECULES AND USES THEREFOR
;  FILE REFERENCE: MNI-108CP2
;  CURRENT APPLICATION NUMBER: US/09/972,473
;  CURRENT FILING DATE:   2001-10-04
;  [Priority information omitted]
; SEQ ID NO 4
;   LENGTH: 848
;   TYPE: DNA
;   ORGANISM: Homo sapiens
;   FEATURE:
;   NAME/KEY: CDS
;   LOCATION: (125)..(796)
US-09-972-473-4

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Query Match 94.5%; Score 638.2; DB 3; Length 848;
Best Local Similarity 96.6%; Pred. No. 8.5e-200;
Matches 652; Conservative 0; Mismatches 23; Indels 0; Gaps 0;

[illegible]

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Qy      421 GAGGGAGAAAGTTGTCTGAGAACTTTTGGACTGTGGCCCTGGACTTTGCTGTGCTCGTCAT480
          |||
Db      545 GAGGGAGAAAGTTGTCTGAGAACTTTTGGACTGTGGCCCTGGACTTTGCTGTGCTCGTCAT604

Qy      481 TTTTGGACGAAAAATTTGTAAGCCAGTCCTTTTGGAGGGACAGGTCTGCTCCAGGAGAGGG540
          |||
Db      605 TTTTGGACGAAAAATTTGTAAGCCAGTCCTTTTGGAGGGACAGGTCTGCTCCAGAAGAGGG664

Qy      541 CATAAAGACACTGCTCAAGCTCCAGAAATCTTCCAGCGTTGCGACTGTGGCCCGGACTA600
          |||
Db      665 CATAAAGACACTGCTCAAGCTCCAGAAATCTTCCAGCGTTGCGACTGTGGCCCTGGACTA724

Qy      601 CTGTGTCTGAAGCCAATGACCAGCAATCAGCAGCATGCACGGTTACGAGTATGCCAAAAA660
          |||
Db      725 CTGTGTCTGAAGCCAATTGACCAGCAATCGGCAGCATGCTCGATTAAGAGTATGCCAAAAA784

Qy      661 ATAGAAAAGCTATAA 675
          |||
Db      785 ATAGAAAAGCTATAA 799

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The prior art sequence, therefore, contains multiple occurrences of “a nucleotide sequence as set forth in SEQ ID NO:1” as recited in the instant claims. Likewise, the 20030068312 application discloses SEQ ID NO: 5, a polypeptide which is 95.5 % identical to SEQ ID NO:2, as shown by the following alignment:

US-09-972-473-5

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; Sequence 5, Application US/09972473
; Publication No. US20030068312A1
; GENERAL INFORMATION:
; APPLICANT: McCarthy, Sean A.
; TITLE OF INVENTION: NOVEL HUMAN DICKKOPF-RELATED PROTEIN AND NUCLEIC ACID
; TITLE OF INVENTION: MOLECULES AND USES THEREFOR
; FILE REFERENCE: MNI-108CP2
; CURRENT APPLICATION NUMBER: US/09/972,473
; CURRENT FILING DATE: 2001-10-04
; [Priority information omitted]
; SEQ ID NO 5
; LENGTH: 224
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-972-473-5

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Query Match          95.5%; Score 1178; DB 3; Length 224;
Best Local Similarity 95.5%; Pred. No. 1.7e-103;
Matches 214; Conservative 4; Mismatches 6; Indels 0; Gaps 0;

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Qy      1 MAAAVLLGLSWLCSPLGALVLDFFNNIRSSADLLGARKGSQCLSDTDCNTRKFCLQSHNEK 60
          | |||
Db      1 MVAAVLLGLSWLCSPLGALVLDFFNNIRSSADLHGARKGSQCLSDTDCNTRKFCLQPRDEK 60

Qy      61 PFCATCRGLQRRRCQRDAMCCPGTLCMNDVCTTMEDATPKLERQLDEQDGTAEVTTGHPV 120
          |||
Db      61 PFCATCRGLRRRCQRDAMCCPGTLCVNDVCTTMEDATPILERQLDEQDGTAEVTTGHPV 120

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Qy      121 QENQPKRKPSIKKSQGRKGQEGESCLRTFDCGPGGCCARHFWTKICKPVLLLEGQVCSRRG 180
          |||
Db      121 QENQPKRKPSIKKSQGRKGQEGESCLRTFDCGPGGCCARHFWTKICKPVLLLEGQVCSRRG 180
          |||

Qy      181 HKDTAQAPEIFQRCDGPGLLCRSQTLSNQGHARLRVCQKIEKL 224
          |||
Db      181 HKDTAQAPEIFQRCDGPGLLCRSQTLSNRQGHARLRVCQKIEKL 224
          |||

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This prior art sequence, therefore, contains multiple occurrences of “an amino acid sequence as set forth in SEQ ID NO:2” as recited in the instant claims.

4. Instant claim 10 is drawn to a method for producing a cynomolgus monkey Dickkopf-4. As “cynomolgus monkey Dickkopf-4” is not recited in the claim to comprise the sequence set forth in SEQ ID NO:2, the structural scope of this term must be found in the specification, which, in turn, states that the cDkk-4 protein of the invention has *an* amino acid sequence as set forth in SEQ ID NO:2 ([0017] in the published application). As noted above, this definition does not exclude the polypeptide of SEQ ID NO:5 in McCarthy. McCarthy teaches production of the disclosed polypeptide by recombinant expression [0014, 0132], thereby anticipating the method of instant claim 10.
5. This rejection could be overcome by amending the indefinite articles “a” and “an” to “the” in claims 1, 5, and 6, and by reciting the amino acid sequence set forth in SEQ ID NO:2 in claim 10.
6. Claims 11, 12, 14, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Application Publication 20040038860 (Allen), filed May 17, 2002. The instant claims are drawn to a method wherein the ability of an analyte to decrease binding of determining of cynomolgus monkey Dickkopf-4 to a Dkk-4 receptor is determined to indicate whether the

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analyte is an antagonist of Dickkopf 4. As noted, the generic recitation of “cynomolgus monkey Dickkopf-4” does not distinguish the claimed polypeptide from Dkk-4 polypeptides in the prior art, in the absence of specific recitation of the amino acid sequence set forth in SEQ ID NO:2. Allen teaches a method for identifying compounds which modulate Dkk and LRP5/LRP6/HBM interactions (see claim 64 and [0129-0133]). The method comprises use of a Dkk fusion protein comprising a fluorescent tag, as recited in instant claim 14 and 15. Allen teaches that “Dkk proteins”, includes Dkk-4 [0019]. Method taught by Allen relies on Resonance Energy Transfer and thus would detect a reduction in binding (as instantly claimed), as well as more subtle disruptions in molecular interaction.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent

Application Publication 20040038860 (Allen) as applied to claims 11, 12, 14, and 15 above, and further in view of Mao et al., Nature 417: 664-667 (2002) (of record). As noted, Allen teaches a method for identifying compounds which modulate Dkk and LRP5/LRP6/HBM interactions, which anticipates the general method of instant claim 11. Allen does not teach,

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however, and embodiment of the method wherein the Dkk receptor is kremen1 or kremen2, as required by instant claim 13. Neither the prior art nor the instant specification provides a direct demonstration that kremen proteins are receptors for Dkk-4. Mao *et al.*, teach that kremen proteins are receptors for Dkk-1 and Dkk-2. Claim 13 relies on the expectation that Dkk-4 will act in a similar fashion to the characterized Dkk proteins and that kremen proteins will perform in a binding assay in a manner similar to LRP5/6. The expectation of success must be high, or the claim would not be enabled by the specification. That is, the use of kremen instead of LRP5/6 in a method similar to that taught in Allen, is an example of choosing from a finite number of solutions with a reasonable expectation of success. It would be, therefore, prima facie obvious for one of skill in the art to modify the assay taught by Allen by using kremen proteins instead of LRP5/6 to arrive at the method of claim 13.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C. Gamett, PhD., whose telephone number is (571)272-1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571 272 0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DCG

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18 January 2008

/David S Romeo/

Primary Examiner, Art Unit 1647